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ABSTRACT

This fact sheet from the National Clearinghouse for Drug Abuse Information discusses methadone, a therapeutic drug for the treatment of narcotic addiction. It reviews the pharmacology of the drug as well as physiological and psychological effects, patterns of use, and adverse effects (toxicity and poisoning). It examines the success rates of inpatient and ambulatory detoxification programs, and, in addition, establishes many differing viewpoints on the success of methadone maintenance. Generally, detoxification programs have not been overly promising, and maintenance programs have varied in their success. The report presents negative opinions about the use of methadone, ranging from cautious criticism to total opposition, in addition to a bibliography. (Author/PC)

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report series

NATIONAL CLEARINGHOUSE FOR DRUG ABUSE INFORMATION

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The National Clearinghouse for Drug Abuse Information recognizes the need for clarifying some of the more complex issues in drug abuse by gathering the significant research findings on each subject and developing fact sheets on the problem. These fact sheets, which are part of the Clearinghouse Report Series, present information about treatment modalities, the pharmacology and chemistry of the various drugs of abuse, and opinions and practices of recognized authorities in the field. This publication was researched and written by James R. Gamage and E. Lief Zerkin of the Student Association for the Study of Hallucinogens (STASH), Beloit, Wisconsin, under Contract No. HSM-42-72-231.

METHADONE: THE DRUG AND ITS THERAPEUTIC USES IN THE TREATMENT OF ADDICTION

Methadone, chemically known as dl-4,4-diphenyl-6-dimethylamino-3-heptanone hydrochloride, was first synthesized by the Germans during World War II. The drug was uncovered by an intelligence team of the U.S. Department of Commerce during the course of an investigation of the German pharmaceutical industry shortly after the war. Methadone has been referred to by a variety of other names, including dolophine, adanone, amidone, physeptone, miadone, butalgin, diadone, polamidone, and 10820. In 1947, the Council on Drugs of the American Medical Association established "methadone" as the generic term for this compound.

Early clinical trials established methadone as a potent analgesic which possessed many of the pharmacologic actions of morphine. In 1949, studies by Isbell and Vogel revealed that methadone had a marked addiction liability. They noted that the drug "in sufficient doses produces a type of euphoria which is even more pleasant to some morphine addicts than is the euphoria produced by morphine."

Despite this early clinical evidence, however, notices in the American lay press soon heralded the discovery of methadone as a breakthrough in addiction treatment. A story published on October 19, 1947, for example, claimed that methadone "does not produce the euphoria, the feeling of exaltation which comes to the addict from cocaine or other (sic) narcotics" and, further, that "it is the safest narcotic drug yet produced."

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Fortunately, physicians were quick to heed the warnings of Isbell and his colleagues, and the widespread use of methadone in the indiscriminate treatment of narcotic addiction was avoided, as were thousands of potential medical addicts that might have been created had clinicians prescribed the drug in the belief that it was a nonaddicting analgesic.

Interest in the clinical applications of methadone did not develop rapidly. In 1952, Davis et al. reported their results in 2,000 deliveries at Chicago's Lying-In Hospital after varying doses of methadone for obstetric analgesia. In doses which produced effective pain relief, however, methadone was found to abnormally depress respiration in the newborn. This study confirmed earlier impressions of Lund (1948), who abandoned methadone in obstetrics after a very short trial. Early interest also developed with regard to the drug's antitussive cough suppressing possibilities. However, because the addiction liability of methadone eventually came to be regarded as far in excess of that of codeine, the latter drug remained preferable in treating cough. For relief of pain, in situations where subcutaneous or other injection routes are contraindicated, methadone became the analgesic of choice largely because it is much more effective in oral preparations than is morphine and other narcotics.

At the present time the approved uses of methadone are limited to analgesia in severe pain, and detoxification and maintenance treatment for narcotic addiction. Because of the increasing incidence of illicit use and abuse of methadone in recent years, the Food and Drug Administration has placed tighter restrictions on its use.

By far the greatest interest in methadone, however, has centered around its use in the chemotherapy of narcotics addiction. In this regard, methadone is viewed as potentially a most beneficial tool for detoxification and long-term maintenance of individuals addicted to heroin and other opiates. The therapeutic potential of methadone will be addressed in the second half of this review, following a short survey of the drug's pharmacology, physiological and psychological effects, patterns of use, adverse effects and toxicity.

Pharmacology

The main pharmacological properties of methadone are qualitatively similar to those of morphine. Methadone's most valuable action is its production of analgesia, or insensitivity to pain. As is the case with most other narcotics, analgesic activity is accompanied by sedation, depression of respiration and central nervous system activity, as well as relaxation of smooth muscle.

When administered parenterally, 7.5 to 10 milligrams (mg.) of methadone produces a degree of analgesia equivalent to that seen after 10 mg. of morphine. Methadone, in equianalgesic doses, has less of a hypnotic action than does morphine, but this difference becomes less marked after chronic administration. Like morphine, methadone readily produces hyperglycemia (high blood glucose concentrations), hypothermia (less than normal body temperature), and the release of antidiuretic hormone.

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Methadone is rapidly absorbed after oral or subcutaneous administration; significant concentrations of the drug can be found in plasma within 10 minutes of injection. Like most other narcotic analgesics, methadone quickly leaves the blood and localizes in the lung, liver, kidney, and spleen. Only a small fraction of the administered dose passes the blood-brain barrier; the highest levels of concentration in the brain occur about 1 or 2 hours after administration.

Methadone undergoes extensive biotransformation, chiefly in the liver; only 10 percent of the administered dose is recovered unchanged in the urine and feces. As early as 1950, Eisenbrandt and his colleagues established that methadone readily crosses the placental barrier and enters into fetal circulation. In this regard, it has been known for some time that infants of mothers who have been maintained on methadone during pregnancy may display narcotic withdrawal symptoms after birth.

Tolerance to the analgesic, nauseant, anorectic, miotic, sedative, respiratory depressant and cardiovascular effects of methadone develops markedly, but at a slower pace than with morphine; however, tolerance to methadone's constipating actions does not readily develop. Individuals tolerant to methadone will also be tolerant to the actions of other narcotic drugs (a phenomenon termed "cross-tolerance"). As such, a patient receiving a high dose of methadone (80 to 120 mg.) per day will typically have little or no subjective or physiological reaction to a shot of illicit heroin, considering the low percentage available on the street.

Isbell and Vogel (1949) have established that physical dependence upon methadone can develop in individuals who receive the drug for as little as 56 days; very little evidence of an abstinence syndrome was observed in three trial subjects who had received methadone for only 28 days. The abstinence syndrome which developed following abrupt withdrawal of methadone was slower in onset, milder, but more prolonged than abstinence from morphine. In general, Jaffe (1965) has noted that the "character and severity of the withdrawal symptoms that appear when a narcotic is discontinued depend upon many factors, including the particular drug, the total daily dose used, the interval between doses, the duration of use, and the health and personality of the addict."

The symptoms of methadone withdrawal generally take longer to appear (8 to 24 hours after the last dose) than those of morphine withdrawal (4 to 6 hours after the last dose). The peak of symptom intensity in methadone abstinence is generally reached on the 6th day, compared to 1½ to 2 days for morphine and heroin withdrawal. The symptoms subside gradually after the 6th day and are minimal by the 10th to the 14th day, although lethargy and anorexia may persist for longer periods.

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Physiological and Psychological Effects

Methadone is a depressant of the central nervous system; the drug also depresses respiration and, in man, produces constipation, probably because it markedly inhibits intestinal tone. Like meperidine, methadone induces relaxation of strips of isolated intestine and inhibits the spasmogenic effect of acetylcholine and histamine in such preparations. *In vivo* (in living systems), however, methadone acts like morphine and produces an increase in intestinal tone, accompanied by diminished amplitude of contractions and marked decrease in the propulsive activity of the intestine.

Methadone produces no marked cardiovascular actions; peripheral vasodilation may occur, producing mild hypotension. The neurophysiological actions of methadone are not significantly different from those of morphine; the electroencephalogram (EEG) exhibits a shift toward increased voltage and lower frequencies, resembling those seen in natural sleep. Like morphine, methadone produces constriction of the pupil size in man, but despite much investigation, the exact mechanism of action in this regard remains unknown.

The subjective effects following single doses of methadone in nontolerant individuals do not differ markedly from those seen after heroin or morphine. In fact, Isbell and Vogel (1949) have remarked that some ex-addicts familiar with the effects of morphine, prefer the euphorogenic actions of methadone. In general methadone produces feelings of well-being, euphoria, drowsiness and other narcotic-like actions.

Patterns of Use

Although methadone is not the drug of choice among American narcotic addicts, its use on the street has been increasing. In 1968, Sapira and his colleagues discovered that 214 out of some 3,000 patients admitted to the U.S. Public Health Service Hospitals at Lexington, Kentucky, and Fort Worth, Texas, were primary methadone addicts. Compared to all other narcotic addicts (primarily heroin users), methadone addicts tended to be older, white, and residing in what the authors termed the "methadone belt" (Virginia, Tennessee, Georgia, Alabama, Mississippi, Louisiana, Arkansas, Oklahoma, New Mexico, and Nevada).

With the widespread proliferation of methadone maintenance and detoxifications programs seen in the past 5 years, however, the issue of "drug program abuse" and the consequent increased availability of methadone on the illicit market has taken on greater importance. An entire workshop on this subject was held at the Fourth National Conference on Methadone Treatment and it was concluded that diversion of medication, missed medication, lost medication, medicine supplementation, multiple registrations of patients and other forms of program abuse do exist throughout the nation.

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Because the administrators of most programs feel that as a patient begins responding to the medication and to the ancillary services (as he "gets better" and is more cooperative and productive), he should not be required to come to the clinic as frequently, the need for "take-home" medication has increased. Placing more responsibility on the patient is regarded as having therapeutic value, in addition to the benefit of freeing more clinic space and staff for less routine matters.

A study by Chambers and Inciardi (1972) disclosed that of 95 active heroin addicts not in treatment, 87 (92 percent) reported that they had been offered the opportunity to purchase illicit methadone within a 6-month period. Of these 95 addicts, 53 (56 percent) admitted to the purchase of illicit methadone on the street, the majority of these 53 buyers (79 percent) reported that methadone was always available in their neighborhoods. The reported source of most of the illicit methadone was from ambulatory patients enrolled in programs which dispensed "take-home" methadone.

In general, tighter program controls on the dispensation of methadone are regarded as the most effective method of preventing the diversion of the drug to the street market. In December, 1972, the Food and Drug Administration issued new, more stringent regulations regarding the use and distribution of methadone. Under the new regulations, new patients must ingest their methadone medication daily, under observation, for at least 3 months before take-home medication may be dispensed. Then only a 2-day take-home supply may be dispensed. After 2 years in the program and progressive rehabilitation, a 3-day take-home supply may be dispensed.

Adverse Effects, Toxicity and Poisoning

In studies with 209 patients enrolled in a methadone maintenance program in New Orleans, Bloom and Butcher (1971) were able to arrive at the following list of the most common untoward reactions to methadone: weight gain (reported by 80 percent), constipation (70 percent), increased intake of fluids (63 percent), delayed ejaculation (60 percent), increased use of alcohol (40 percent), increased frequency of urination (37 percent), numbness of hands and feet (32 percent), and hallucinations (17 percent). A subsequent study by Goldstein (1971) disclosed a similar list of adverse effects; an additional complaint, excessive sweating, that did not seem to be related to dosage, also turned up.

Goldstein (1971) did point out, however, that "almost without exception, the body symptoms complained of on methadone were present prior to starting on the program, when the patient was using heroin. Most of these improved on methadone, so that despite the natural tendency to blame all troubles on the drug one happens to be taking, it is difficult to classify them as side effects."

Like most other narcotics, methadone toxicity varies with the individual and the degree of tolerance built up to the opiate drugs. Acute methadone poisoning may result from clinical overdosage, accidental overdosage in addicts (or relatives who may take oral methadone preparations by mistake) or suicidal attempts. By the time

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the patient reaches medical assistance, he may be asleep or stuporous; if a large overdose has been taken he may lapse into a profound coma from which he cannot be aroused. The principal danger of methadone overdose is diminished pulmonary ventilation; the respiratory rate may be as low as 2 to 4 per minute and cyanosis may be present. Treatment involves the administration of nalorphine in intravenous doses of 3 to 5 mg., judiciously over the course of 20 to 30 minutes. Naloxone hydrochloride (Narcan), which is 10 to 30 times as potent as nalorphine, is becoming the drug of choice in situations where an opioid antagonistic effect is required. Unlike nalorphine, naloxone has no depressant qualities of its own.

The primary precaution to be stressed in the management of methadone poisoning with antagonists is the necessity for continuous, prolonged monitoring of the patient's vital functions. Because the duration of action of methadone is much longer than the duration of action of nalorphine (or other antagonists), a patient may respond well immediately after treatment, only to lapse into a coma several hours later, when the effect of the antagonist has worn off but the action of the agonist persists. Treatment with antagonists may be required for up to 24 hours or more, whenever signs of lethargy occur.

Methadone in the Management of Narcotics Addiction

The two major modalities which employ methadone for the management of narcotics addiction are detoxification and maintenance. Methadone has been used in a variety of different ways in both modalities and, at times, the line distinguishing detoxification from maintenance has not always been clearly drawn. The methadone regulations issued by FDA in December, 1972 define detoxification treatment and maintenance treatment as follows:

> "Detoxification treatment" using methadone is the administering or dispensing of methadone as a substitute narcotic drug in decreasing doses to reach a drug free state in a period not to exceed 21 days in order to withdraw an individual who is dependent on heroin or other morphine-like drugs from the use of these drugs.
>
> "Maintenance treatment" using methadone is the continued administering or dispensing of methadone, in conjunction with provision of appropriate social and medical services, at relatively stable dosage levels for a period in excess of 21 days as an oral substitute for heroin or other morphine-like drugs, for an individual dependent on heroin. An eventual drug free state is the treatment goal for patients but it is recognized that for some patients the drug may be needed for long periods of time.

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Isbell and Vogel (1949) were the first to study the effectiveness of methadone in the chemotherapy of narcotic detoxification. Their clinical experience encouraged the United States Public Health Service Hospitals at Lexington, Kentucky, and Fort Worth, Texas, to adopt methadone as the most satisfactory method of allaying narcotic withdrawal hunger in the process of weaning addicts from opiates. The initial regimen called for the subcutaneous injection of methadone twice daily. The amount of the drug was decreased in graded amounts over a 7 to 10 day period, after which a physiologically detoxified state (lack of physical dependence) was achieved by the addict.

Since the early 1950's, however, various techniques employing methadone in the detoxification of addicts have evolved. Chambers (1973) has grouped these techniques into two major categories: inpatient withdrawal and ambulatory (or outpatient) detoxification. Both of these techniques require certain basic adjustments to make the treatment appropriate to the patient, including modifications that take into consideration: (1) amount of heroin habitually used; (2) the existence of multiple drug dependency involving hypnotics, alcohol, or minor tranquilizers; and (3) the patient's overall physical and psychiatric condition.

Proponents of inpatient methadone withdrawal generally assert that addicts present themselves not only with a drug-dependency problem, but with a multiplicity of psycho-social disorders as well. These external conditions are often viewed as the major underlying causes of the drug-dependency problem and figure importantly in the high relapse rates seen in patients following withdrawal. The goal of inpatient withdrawal is, therefore, to help an individual reach a drug-free state in a supportive and closely supervised environment which, for a limited time at least, protects him from the adverse pressures of the street. During this process it is hoped that the program will be able to provide adequate ancillary services (such as counseling, job placement, etc.) and that, once drug-free, the patient will be more likely to become a productive member of society.

The philosophy of ambulatory withdrawal programs shares many characteristics with that of the inpatient technique. The first major goal is to stabilize the patient on a low to moderate dose of methadone (20 to 40 mg. per day) and then to gradually reduce the dose until such time as the addict-patient no longer requires the administration of a narcotic to allay withdrawal discomfort. During the treatment process a great deal of stress is placed upon helping the addict to learn new or reestablish old productive behavioral patterns. However, the ambulatory methadone detoxification technique more than any other, requires the patient to assume the largest share of responsibility for treatment and rehabilitation success. The physician's role is decidedly more passive than in inpatient detoxification; he can only administer medication and provide supportive services if the addict-patient decides to come to the clinic. During the course of withdrawal, the patient must, in fact, make a

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series of decisions to come back for treatment and in this sense, ambulatory detoxification becomes a social-interaction and motivational process while inpatient withdrawal is more of a medical process.

The success rates of inpatient and ambulatory detoxification programs have not been overly promising. Chambers et al. (1973) assert that cheating, primarily in the form of self-administration of heroin and other illicit drugs, can be expected from at least 50 percent of patients who enroll themselves in detoxification programs. The experience of most programs is that anywhere from 40 to 70 percent of patients drop out of therapy against medical advice. Of those who complete detoxification procedures, less than half typically stay "clean" of illicit drug use for any appreciable length of time. For example, a post-treatment behavioral study conducted by Moffett and his colleagues (1973) disclosed that the total relapse rate for patients who left against medical advice and for those who remained in the program was 89.1 percent. As expected, the rate of return to opiate use was greater for the group that left against advice, but at the end of 6 months only 9.5 percent of those who had completed medical withdrawal remained drug-free.

Methadone Maintenance

While the detoxification procedures described above subscribe to the goal that total, immediate abstinence must be the starting point and sine qua non of all rehabilitation, methadone maintenance, in the varying forms in which it is practiced throughout the United States, attempts to shift emphasis to social and vocational rehabilitation.

There are several historical precedents which support such a shift of philosophical emphasis away from abstinence per se as the desirable end goal of the treatment process. In 1912 and 1913, clinics which dispensed narcotics legally to addicts were established in Florida and Tennessee. According to Brecher (1972), "Following the passage of the Harrison Narcotic Act in 1914, clinics for supplying addicts with legal heroin at low cost or without charge spread throughout the country; at least 44 of them are known to have been opened by 1920 or 1921." Heroin maintenance has also played an important role in the so-called British "System" of narcotics treatment. In reality, there are several British systems of narcotic rehabilitation, some stressing detoxification, and some placing an emphasis on social productivity as a condition for obtaining maintenance drugs.

The origin of the use of methadone in the maintenance of narcotics addicts is generally attributed to Dr. Vincent P. Dole, who in the 1950's primarily occupied himself with metabolic studies of obese patients. In a number of respects, Dr. Dole was able to draw parallels between obese individuals and narcotic addicts: they both exhibited an overwhelming craving for their "drugs" (food or heroin) and the tendency of obese patients to relapse after dieting also resembled the proclivity of heroin addicts to return to drug use following detoxification. The result of Dr. Dole's studies on overweight individuals led him to formulate a theory which linked the "disease" of

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obesity to profound alterations in metabolism. When Dr. Dole turned his energies to the study of heroin addiction, he naturally began to focus on the metabolic aspects of what he regarded as a potentially similar type of biochemical disorder.

In collaboration with Dr. Marie Nyswander, Dole began a series of metabolic investigations of chronic morphine use. As a part of the studies the patients were allowed to increase their doses as they pleased, and within three weeks they were requesting and receiving eight shots totalling 600 mg. of morphine per day. In this short time, morphine had become the center of their lives: "Much of the time they sat passively, in bathrobes, in front of a television set. They didn't respond to any of the other activities offered them. They just sat there, waiting for the next shot" (Brecher 1972).

After the metabolic tests were concluded, the doctors prepared to detoxify their patients by switching them over to equally potent doses of oral methadone. Instead of proceeding immediately with withdrawal procedures (which would normally allow patients to become drug-free in about 10 days), Dole and Nyswander allowed them to remain on high doses of methadone while additional comparative metabolic tests were conducted. During the course of these additional metabolic studies, however, dramatic spontaneous changes in the behavior of the patients were observed. Instead of sitting around, nodding lifelessly and waiting only for their next dose of the narcotic, one of the older addicts began to paint industriously and another patient urged the clinical team to let him get his high school equivalency diploma. Soon both the patients began to attend school outside the hospital grounds, though they returned to the institution at night to receive their medication. After a short time on methadone maintenance they had become, in the eyes of Dole and Nyswander, "normal, well-adjusted, effectively functioning human beings--to all intents and purposes cured of their craving for an illegal drug" (Brecher 1972).

These same results were replicated when an additional four hard-core addicts were placed on experimental methadone maintenance in 1964. Shortly after these early clinical trials, Dole and Nyswander obtained inpatient beds at the Manhattan General Hospital (which has since become the Beth Israel Medical Center) and launched a broader investigation into the potentials of methadone.

The methadone maintenance modality, as it was developed by Dole and Nyswander, was based on the assumption that during the development of addiction to heroin, certain dramatic metabolic changes took place in the addict. The paradigm employed to justify medically supervised maintenance with methadone was that of the insulin requirement of the diabetic. According to Chambers and Brill (1973), "Basic to this model was the feeling that there exists no proof of prior psychological or social etiological problems in confirmed addicts, and that much of the psychopathic and acting-out behavior observed is a consequence, rather than a cause, of addiction." In an oversimplified view, once methadone was able to relieve the "metabolic deficiency" that had developed during the course of addiction to heroin, the person could function normally.

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Another concept basic to the original Dole-Nyswander methadone model is that of "narcotic blockade." It is supposed that if high enough doses of methadone (80 to 120 mg. per day) are given to patients, they will develop a physiological state of "blockade" in which all opiate receptors in the body are occupied by methadone. In this state, the methadone maintained individual will be "immune" to any effects from all but extraordinarily large subsequent doses of other narcotics.

After a period of more intensive study, Dole and Nyswander outlined the following advantages of methadone over other potential forms of narcotic maintenance: (1) the drug can be taken orally; (2) it has an extended duration of action (from 24 to 36 hours); (3) no serious side effects are seen at maintenance doses; (4) at sufficient dose levels, methadone will "block" the effects of heroin; and, (5) administered therapeutically and orally, methadone does not produce euphoric effects of its own after tolerance has been established; therefore the patient is able to function normally.

The original Dole-Nyswander program accepted addicts for treatment only if they met the following criteria: (1) that they volunteer for the program; (2) that they are between 20 and 40 years of age; (3) that they have a history of at least 4 years of "mainline" heroin use with repeated relapses following detoxification; and (4) that they have no concurrent dependencies on non-narcotic drugs such as alcohol, barbiturates, or minor tranquilizers. Following admittance, patients were hospitalized for a period of 6 weeks, during which time they received thorough medical and psychiatric examinations and were gradually stabilized on a "blockading" dose of methadone. Small divided doses of 10 to 20 mg. per day of the oral drug preparation were slowly increased, as tolerance permitted, to a stabilization level of 80 to 120 mg. per day. At the termination of the 6-week inpatient period, patients were given their high-dose methadone daily on an outpatient basis. Urine specimens were taken regularly to monitor any relapses into illicit drug use.

The results of Dole and Nyswander's early clinical studies were promising. Just over two-thirds of the total of 3372 patients enrolled were retained in the treatment program at the end of a 42-month evaluation period. Those who left the program against medical advice were more likely to suffer arrest and readdiction, while those who were discharged voluntarily more often entered other forms of treatment, had fewer arrests and were better adjusted socially. Approximately 33 percent of those who left treatment voluntarily decided to reenter the methadone maintenance program at a later date. Two cautionary notes must be added, however. The arrest statistics were compiled from self-reports of patients and may not be a highly valid measure of criminal activity; and approximately 10 percent of those in the program took up the abuse of potent non-narcotic drugs, such as alcohol, barbiturates, and cocaine, with the result that many had to be eventually discharged from treatment.

Because of the encouraging results of the initial studies, methadone maintenance was believed to be an important means of reducing crime in communities with high

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rates of drug addiction. A recent evaluation of the results of the methadone treatment program at St. Luke's Hospital Center in New York City lends support to this view. City police records for 119 patients enrolled in the program showed that the arrest rate fell by 93 percent during treatment. Cushman (1973) stated that "Not only were the arrest rates reduced appreciably during treatment, but the pattern of arrests also changed impressively...It was predominantly arrests for crimes involving narcotics, prostitution and money that were greatly decreased during treatment."

After a review of the results of Dole and Nyswander's pioneer methadone program by the American Medical Association's Methadone Maintenance Evaluation Committee, it was concluded that "...those who remain in the program have, on the whole, become productive members of society in contrast to their previous experience, and have, to a large extent, become self-supporting and demonstrate less and less antisocial behavior" (Methadone Maintenance Evaluation Committee 1968).

Other researchers have instituted methadone maintenance programs either to replicate the Dole-Nyswander results in other locations with different staffs or to attempt to modify the procedures and admissions criteria. The most significant modifications made to date have involved carrying out the stabilization procedure on an outpatient basis and the use of lower doses of methadone for maintenance purposes.

As other programs formed throughout the Nation, many clinicians believed that they were seeing large numbers of addicts who appeared not to need either high doses of methadone or prolonged maintenance. For example, Brill (1973) reports that in the Philadelphia program, drug craving for several patients could be suppressed at low-dose levels of up to 40 mg. of methadone per day. It is believed that these patients utilized methadone in a different manner than the high-dose patients of the Dole-Nyswander program: the drug seemed to serve as a kind of tranquilizer or anti-depressant which enabled patients to achieve a somewhat calm state while attempting to reconstruct their lives. It was conservatively estimated that at least 20 percent of the addicts who present themselves for treatment in Philadelphia are able to benefit from such low-dose regimens.

When low-dose maintenance was employed strictly on an outpatient basis, the Philadelphia researchers concluded that numerous advantages accrued. For example, the addict is allowed to remain in his community and is not required to sever, for six weeks, whatever constructive relationships may exist in the form of employment, family or community ties. Also, from a simple cost standpoint, the ambulatory methadone maintenance modality is far less expensive to operate than one which requires institutionalization and scarce hospital beds. Futhermore, a comparison of low-dose ambulatory patients with patients who had entered the regular Dole-Nyswander type of program revealed that, in selected cases, outcomes were not significantly different. The authors concluded that the "dosage per se was less

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important than other factors such as typology of patients, ancillary services, and attitude of the program staff."

Additional doubt has been shed both on the "metabolic" theory of heroin addiction and its consequent requirement for high doses of methadone by research conducted by Goldstein (1972). In the first place, Goldstein notes that "relapses to heroin use from abstinence (or from being "clean" on methadone) are episodic, unlike what would be expected in a metabolic disease. A specific event, such as meeting an old addict friend, returning from incarceration to the scene of former connections, or even reading about narcotics, triggers a sudden flood of memories, an intensive feeling of 'being sick' and an irresistible compulsion to use again." Goldstein goes on to argue, based on the results of recent studies of narcotics relapse, that "these aperiodic overwhelming compulsions to use heroin, which occur in patients maintained on methadone as well as in totally abstinent ex-addicts, are much more convincingly explained by conditioning theory, particularly as elaborated by Wikler, than by a 'biochemical need' for opiates."

Goldstein and many others also prefer the concept of "cross-tolerance" to "blockade" to describe the action of methadone in preventing euphoric reactions to subsequent self-administrations of heroin or morphine. In this regard, Goldstein has established that doses as low as 30 mg. per day are sufficient to induce a marked cross-tolerance to heroin. Further, in blind tests with 40, 80 and 160 mg. per day, he found that the subjective differences in doses were generally very small or absent.

Goldstein (1972) has stated that "although different doses in the same program lead to the same degree of success or failure, the same dose in different programs can lead to very different results. Methadone cannot magically prevent heroin use in a patient who wants to use heroin; it can only facilitate a behavior change in people who have made a conscious decision to change. Thus, the paramount feature of a successful methadone program is what it does in ways other than chemical to help the patient rehabilitate himself."

More and more clinicians and researchers, like Goldstein, are calling for expanded research into the potentials of methadone. Much of this research will hopefully focus on the development of new treatment modalities employing the drug. For example, the concept of methadone temporary support has begun to generate considerable interest; it calls basically for making fixed low-dose (30 to 50 mg. per day) short-term maintenance available to ambulatory addicts and others who would not ordinarily be interested in long-term maintenance or short-term detoxification. Slow withdrawal would be carried out as a matter of course after 6 months or a year of intensive treatment, during which time the patient would be brought into therapeutic contact with a number of medical, psychiatric and social rehabilitation resources.

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Despite the overwhelmingly favorable reaction that methadone maintenance has received in the lay press and among certain professionals, others have voiced negative feelings, ranging from cautious criticism to out-and-out opposition. An example of the former reaction is the following excerpt from the Sixteenth Report of the World Health Organization's Expert Committee on Drug Dependence:

> Methadone maintenance for drug dependence of the morphine type remains experimental...and has not yet been adequately evaluated. The techniques of well-designed clinical drug trials including scientifically controlled series and/or comparison groups are required on these trials. It is important that the influence of factors other than methadone itself be evaluated....To date, patients involved have, in the main, been highly motivated, carefully selected and provided with organized aftercare arranged so as to develop a supportive group process. Furthermore, these patients have not been shown to be a representative sample of the drug-dependent population in other respects: e.g., age, ethnic grouping and educational level. Finally, it must be not forgotten that methadone itself is a drug of dependence and that persons taking it regularly in the methadone program continue to have a drug dependence of morphine type.. It will, therefore, be necessary to keep in view the question of final withdrawal of methadone from these patients.
>
> --WHO Expert Committee on Drug Dependence (1969)

Similar cautions were also emphasized in the generally favorable report on methadone maintenance that was issued under the chairmanship of Henry Brill:

> It should be emphasized that these are volunteers who are older than the average addict and may be more highly motivated. Consequently, generalizations of the results of the program in this population to the general addict population probably are not justified.
>
> --Methadone Maintenance Evaluation Committee (Columbia University) (1968)

In contrast to the types of cautionary notes appended to the generally recognized success of methadone in select populations presented above, are criticisms of a more fundamental nature. For example, therapeutic communities such as Synanon, Daytop Village, Phoenix House, Odyssey House, and others, generally hold firm to the belief that immediate abstinence is the most important prerequisite to rehabilitation. In this regard, according to Brill (1973), "They do not see patients on methadone maintenance as any better off than heroin addicts since they are still dependent and 'stoned'; no one can be said to be rehabilitated unless he is completely off drugs."

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From a somewhat different perspective, black militants have also attacked methadone maintenance as "genocide" (because of the belief that methadone has markedly adverse effects on the libido), as "narcotization of the blacks" (Brill 1973). The following excerpt from a monthly newsletter of a black-centered addict rehabilitation center paraphrases many of the attitudes towards methadone among indigenous blacks:

> (Methadone) can "program" the addict population (50,000 strong) to "influence, work, vote" for whoever and whatever agency responsible for maintaining their supply of dope....Methadone endangers social progress...(it) takes a sick dope fiend at a time when he is incapable of thinking for himself and turns him into a "maintained" robot, with no claim of cure....Heroin addiction is spawned among the ghetto problems of the Black Man....Black People make up half of all recorded drug victims. The reduction in the price of heroin from $10 to $2 a bag makes it "conveniently available" to thousands of little Black Chi'dren seeking an "escape." This makes methadone more of an "endorsement" rather than an effort to prevent or curb ghetto addiction. I submit that as addiction increases in the ghetto, Black People will be reduced to the status of "Maintained Black Slaves." ...A methadone maintained person will never be thought of as equal...Methadone is a waste of time, energy, intelligence and money unless we're trying to slowly kill off Black People!
>
> --Reverend James Allen (1969)

A similar view, abhorring methadone as the substitution of one crutch for another, has also been advanced by a white sociologist:

> It is abundantly clear...that one does not cure a craving for heroin-induced euphoria by substituting a methadone-induced euphoria that is euphemistically labelled "stabilization dosage," and by then asserting that this latter state is "normal" and should be perpetuated indefinitely. I fail to appreciate how legalized addiction is any improvement over illicit addiction. Morally, in fact, it is much less defensible, because it indicates that society is actively abetting the well-proven personality deterioration and social demoralization that have invariably accompanied narcotic addiction over the past 50 years.
>
> --David P. Ausubel (1966)

One noted clinician has pointed out that methadone may be used rationally in a number of different ways and that modalities developed which employ the drug do not necessarily have as a consequence the maintenance of permanently addicted individuals:

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> Too much has been made of the false dichotomy "drug free" (right away!) versus methadone maintenance (forever!). We need flexible programs in which patients can move at their own optimal rates from methadone to total abstinence--and freely back to methadone if relapse occurs. A program that gains the confidence of the addicts can become a permanent community resource, to which they can turn again when in need of help. Then no ex-addict, once abstinent, need suffer the hitherto catastrophic consequences of relapse. This concept is analogous to the modern ambulatory maintenance of psychotic patients, with or without medication, as required to keep them functional in the community.
>
> --Avram Goldstein (1972)

Perhaps one of the most sober assessments of the meaning of methadone to addicts in need of rehabilitation as well as to drug program workers and the society at large, has been made in a recent review by two respected psychiatrists in the addiction services field:

> It is too early to expect or to provide a definitive assessment of the role of methadone in the rehabilitation of narcotic addicts. It is thought that some 60,000 persons are now in treatment from a reservoir variously estimated at 250,000 or 650,000. Our current opinion is that programs which offer a wide range of services, and which use methadone in support of their operations, can be useful for some 40 to 60 percent of addicts who volunteer for treatment, and can aid them in achieving a socially desirable change in life style. Physicians should nevertheless be aware of some of the current problems in evaluation in order to appreciate issues that may arise as programs and facilities proliferate.
>
> Confusions of goals, complexity of the range of problems being treated, clashes of values as to the desired treatment outcome, different conceptions of the behavior entailed in addiction, and the consequent inevitable stereotyping and politicization--not only of drugs and the people who use them, but of the appropriate social response to them--are factors complicating sound medical and scientific evaluations. The many players on the stage--the police, community and neighborhood leaders, rehabilitation workers, physicians, ex-addicts, the pharmaceutical industry, the mushrooming private corporations selling packaged services ranging from therapy to the various techniques for urinalysis, various power groups in government from the executive to the Congress, to agencies in the states and cities--hardly provide a scene which can be readily understood.
>
> --Daniel X. Freedman and Edward C. Senay (1973)

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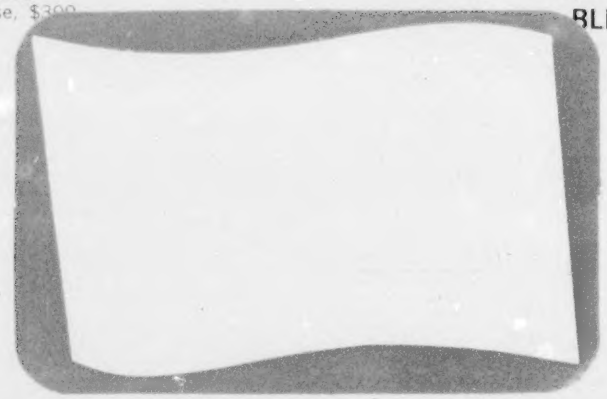

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